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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/619,032	07/19/2000	Dennis Murphy	DIVER1120-3	2212

20985 7590 05/23/2003

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EXAMINER

RAMIREZ, DELIA M

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 05/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/619,032	MURPHY ET AL.
	Examiner	Art Unit
	Delia M. Ramirez	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) Responsive to communication(s) filed on 25 March 2003.

2a) This action is **FINAL**.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) Claim(s) 1-15 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-15 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 25 March 2003 is/are: a) accepted or b) objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.

    If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 17.

4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.

5) Notice of Informal Patent Application (PTO-152)

6) Other: \_\_\_\_\_.

**DETAILED ACTION**

***Status of the Application***

Claims 1-15 are pending.

Applicant's amendment of claims 1-3, 6-7, 9, addition of claims 13-15, and amendments to the specification, in Paper No. 20, filed on 3/25/2003 is acknowledged.

Applicant's submission of a declaration under 37 CFR 1.132 by Mr. Walter Callen, an ATCC international form indicating the deposit of plasmid 18GC, a declaration by Ms. Mi Kim in regard to a biological deposit made under the terms of the Budapest Treaty, a copy of a verified statement under 37 CFR 1.821 submitted in related case 09/886400, and a new sequence listing, in Paper No. 8, filed on 2/19/2003 is acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

***Information Disclosure Statement***

1. The information disclosure statement (IDS) submitted on 1/28/2003 was filed after the mailing date of the first action on the merits on 12/2/2002. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

***Drawings***

2. Figure 1 is objected to because Figure 1, as amended, now shows the first codon, TTG, as encoding an Ile residue instead of a Leu residue. Since TTG encodes Leu and not Ile, it is

assumed that the recitation of Ile in Figure 1 is a typographical error and not an amino acid change. Correction is required.

3. The formal drawings submitted on 3/25/2003 have been reviewed by a draftsperson.

***Claim Objections***

4. Claim 7 is objected to because of the recitation of "the method according to claim 6 wherein the  $\alpha$ -glycosidic bond is in raw beet sugar". For clarity, it is suggested that the claim be amended to recite "wherein the raffinose is in raw beet sugar" to clearly indicate that the claim is further limiting raffinose. Appropriate correction is required.

***Claim Rejections - 35 USC § 112, First Paragraph***

5. Claims 1-12 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This was a new matter rejection.

6. This rejection is discussed at length in Paper No. 16, mailed 12/2/2002.

7. Applicants request that the PTO consider the corrected sequence listing provided in Paper No. 20, filed on 3/25/2003.

8. Upon visual comparison of SEQ ID NO: 4 in Applicant's corrected sequence listing, and the amino acid sequence set forth in Figure 1, it appears that both sequences are the same. The corrected SEQ ID NO: 4 no longer displays a methionine residue as the first residue.

9. In regard to changes in the sequence of SEQ ID NO: 3 as submitted by Applicants in the corrected sequence listing, it is noted that in view of the disclosure of clone 18GC in U.S. Application No. 08/613,220 (now U.S. Patent No. 5958751) which contains the polynucleotide of SEQ ID NO: 3, the submission of Mr. Walter Callen's declaration, an ATCC international form indicating the deposit of plasmid 18GC, a declaration by Ms. Mi Kim in regard to a biological deposit made under the terms of the Budapest Treaty, and the amended sequence listing, it has been determined that the polynucleotide of SEQ ID NO: 3 and the polypeptide of SEQ ID NO: 4 of the instant application are entitled to claim priority back to March 8, 1996, which is the filing date of U.S. Application No. 08/613,220. As such, changes in the sequence of SEQ ID NO: 3 due to re-sequencing, as asserted by Applicants, are not deemed to introduce new matter. This new matter rejection is hereby withdrawn.

10. Claims 1, 3, 5-13, and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of hydrolyzing  $\alpha$ -1,6 galactosyl bonds with the  $\alpha$ -galactosidase of SEQ ID NO: 4, does not reasonably provide enablement for a method of hydrolyzing  $\alpha$ -1,6 galactosyl bonds with an  $\alpha$ -galactosidase which is 70% sequence identical to that of SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

11. This rejection has been discussed at length in Paper No. 16, mailed on 12/2/2002, and it is applied to newly added claims 13 and 15 for the reasons of record.

12. Applicants argue that the amended claims are not directed to a method of hydrolyzing any bond with an enzyme having at least 70% sequence identity to that of SEQ ID NO: 4. Applicants submit that the specification is enabling for the subject matter claimed and that said specification is directed to the skilled artisan who is well versed in biological research protocols. As such, it is Applicant's contention that it would be routine for one of skill in the art to practice the claimed invention. Furthermore, Applicants argue that the focus of the enablement inquiry should be whether the required experimentation is "undue". Applicants cite the Federal Circuit ruling in regard to *Hybritech, Inc. v. Monoclonal Antibodies, Inc.* to support the argument that while some experimentation may be required, this does not constitute undue experimentation.

13. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. While it is agreed that (1) the claims as amended are not directed to a method of hydrolyzing any bond, (2) one of skilled in the art would be well versed in biological research protocols, and (3) some experimentation required may not constitute undue experimentation, the specification is not enabling for the full scope of the claimed invention for the following reasons. The claims as amended and/or added are drawn to a method for hydrolyzing a glycosidic bond with an enzyme having  $\alpha$ -galactosidase activity, wherein said enzyme is at least 70% sequence identical to the polypeptide of SEQ ID NO: 4. As such, one of skill in the art would have to know which are the amino acids which can be modified, i.e. substituted, deleted or added, in the polypeptide of SEQ ID NO: 4 to obtain a 70% structural homolog and still retain  $\alpha$ -galactosidase activity. While the specification discloses the structure of the polypeptide of SEQ ID NO: 4 as well as its function, there is no disclosure of the critical structural elements in said polypeptide which correlate with  $\alpha$ -galactosidase function, nor there

is disclosure of which structural elements in the polypeptide of SEQ ID NO: 4 can be modified without major changes in activity.

The argument can be made that the required enzyme can be isolated by sequence homology using the structures disclosed in the instant specification and the prior art. However, the state of the art teaches the unpredictability of assigning function based on structural homology and also teaches that small structural changes can lead to significant changes in function. See the teachings of Bork, Broun et al., Van de Loo et al. and Seffernick et al. already discussed in previous Office Action Paper No. 16. In addition, Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a  $\beta$ -ketoacyl synthase into a malonyl decarboxylase and completely eliminates  $\beta$ -ketoacyl synthase activity. While the Examiner acknowledges the ruling in *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, in the instant case, in view of the information provided and unpredictability of the art in regard to structural changes and function, one of skill in the art would have to go through the burden of undue experimentation to isolate/make structural homologs of the polypeptide of SEQ ID NO: 4 and determine if they have  $\alpha$ -galactosidase activity. Therefore, one cannot reasonably conclude that the specification provides adequate enablement for the full scope of the claimed invention.

#### ***Double Patenting***

14. Claims 1-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 2 of U.S. Patent No. 5958751.
15. This rejection has been discussed at length in Paper No. 16, mailed on 12/2/2003, and is now applied to newly added claims 13-15 for the reasons of record.

16. Applicants submit that a terminal disclaimer has been filed which would obviate this rejection.

17. It is noted that while Applicants assert that a terminal disclaimer has been filed, the Examiner is unable to locate such terminal disclaimer in the file and the PTO records show no payment of the corresponding fees either. Therefore, the rejection is maintained for the reasons of record.

18. Claims 1-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/114,083.

19. This rejection has been discussed at length in Paper No. 16, mailed on 12/2/2003, and is now applied to newly added claims 13-15 for the reasons of record.

20. Applicants request that any issues in regard to this rejection be deferred until an agreement of the instant claims is reached.

21. Since no arguments have been presented and no terminal disclaimer has been filed, this rejection is maintained for the reasons of record.

### *Conclusion*

22. No claim is in condition for allowance.

23. Applicant's amendment of claims 1-3, 6-7, 9 and addition of claims 13-15, necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS**

**MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

24. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

25. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.  
Patent Examiner  
Art Unit 1652

DR  
May 16, 2003

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